REMARKS

The specification has been amended to provide a unique sequence identification number for each nucleotide sequence within the specification. The attached sequence listing has also been inserted into the application. No new matter is introduced by any of these amendments.

If there are any other charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 3 June 2002

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Michael Hallek et al.	Art Unit:	
Serial No.:	10/031,187	Examiner:	
Filed:	January 18, 2002	Customer No.:	21559
Title:	SCLEROPROTEIN OF AN ADENO-ASSOCIATED VIRUS WITH MODIFIED CHROMATOGRAPHIC PROPERTIES, THE PRODUCTION THEREOF AND USE OF THE SAME		

Assistant Commissioner For Patents
Washington, DC 20231

VERSION WITH MARKINGS TO SHOW CHANGES MADE

A marked up version of the amended fourth full paragraph on page 10 (lines 28-39) of the specification is presented below.

In a further preferred embodiment, the other mutation(s) represent(s) one or more deletions and/or one or more insertions in the structural protein or combinations of said modifications. In this connection, insertion is preferably the insertion of a cell membrane receptor ligand, of a Rep protein or peptide, for example in the form of a Rep domain, of an immunosuppressive protein or peptide and/or of a protein or peptide with a signal for double strand synthesis of a transgene or foreign gene. A preferred example in this connection is the P1 peptide (QAGTFALRGDNPQG) (SEQ ID NO: 1) (see above).

A marked up version of the amended third full paragraph on page 13 (lines 26-33) of the specification is presented below.

In another preferred embodiment, one or more insertions are present in the VP3 structural protein (Rutledge, E.A. et al. (1998) supra) before and/or after at least one amino acid in

the sequence selected from YKQIS SQSGA (SEQ ID NO: 2), YLTLN NGSQA (SEQ ID NO: 3) , YYLSR TNTPS (SEQ ID NO: 4), EEKFF PQSGV (SEQ ID NO: 5), NPVAT (SEQ ID NO: 6), EQYGS (SEQ ID NO: 7), LQRGN RQAAT (SEQ ID NO: 8), NVDFT VDTNG (SEQ ID NO: 9), because these sites are located on the exposed sites of a loop, in which case the risk of altering the VP3 structure is small.

A marked up version of the amended second full paragraph on page 17 (lines 15-23) of the specification is presented below.

Mutations in VP3

a)	ins261; YKQIS SQSGA	(SEQ ID NO: 10)
b)	ins381; YLTLN NGSQA	(SEQ ID NO: 11)
c)	ins447; YYLSR TNTPS	(SEQ ID NO: 12)
d)	ins534; EEKFF PQSGV	(SEQ ID NO: 13)
e)	ins573; NPVAT EQYGS	(SEQ ID NO: 14)
f)	ins587; LQRGN RQAAT	(SEQ ID NO: 15)
g)	ins713; NVDFT VDTNG	(SEQ ID NO: 16)

A marked up version of the amended third partial paragraph on page 22 (lines 26-39) and the first partial paragraph on page 23 (lines 1-8) of specification is presented below.

This shows that insertion of the QAGTFALRGDNPQG (SEQ ID NO: 1) peptide alters the elution behavior of the AAV particles so that, at the same pH, the mutated particles elute at a lower salt concentration than the wild-type particles. This means that the virus fraction is shifted toward other fractions which are in some circumstances less impure or otherwise more suitable. It is therefore possible to alter the chromatographic properties of the AAV particles by insertions, deletions or other modifications of the capsid proteins. It is possible in particular in one variant of the insertion shown to construct, by introducing amino acids with a predominantly positive charge, for example at the insertion sites shown in the examples, capsid mutants of the invention which elute at higher salt concentrations compared with the wild type (which elutes in a broad, less impure peak). The affinity of the mutant for the column material is enhanced thereby, so that elution does not take place until the salt concentrations are high, that is to say in regions which are normally less contaminated by smaller foreign proteins.

In the Claims

A marked up version of claims 37, 58, and 59 are presented below.

37. (Amended) The method as claimed in claim 35, wherein a peptide which has the sequence QAGTFALRGDNPQG (SEQ ID NO: 1) is inserted into the structural protein.

58. (Amended) The method as claimed in claim 27, wherein one or more insertions in VP3 is/are located before and/or after at least one amino acid in the sequence selected from the group consisting of YKQIS SQSGA (SEQ ID NO: 2), YLTLN NGSQA (SEQ ID NO: 3), YYLSR TNTPS (SEQ ID NO: 4), EEKFF PQSGV (SEQ ID NO: 5), NPVAT EQYGS (SEQ ID NOS: 6 and 7), LQRGN RQAAT (SEQ ID NO: 8), and NVDFT VDTNG (SEQ ID NO: 9)

59. (Amended) The method as claimed in claim 38, wherein one or more additional insertion(s) in VP3 is/are located before and/or after at least one amino acid in the sequence selected from the group consisting of YKQIS SQSGA (SEQ ID NO: 2), YLTLN NGSQA (SEQ ID NO: 3), YYLSR TNTPS (SEQ ID NO: 4), EEKFF PQSGV (SEQ ID NO: 5), NPVAT EQYGS (SEQ ID NO: 6 and 7), LQRGN RQAAT (SEQ ID NO: 8), and NVDFT VDTNG (SEQ ID NO: 9).